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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,869	02/13/2002	Paul D. Robbins	AP32573-AAA 072396.0237	9884

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,869	ROBBINS ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 6-14, 17, 42, 45-47 (in-part)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/3/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-2, 5, 6-14, 17, 42, 45-47 (in-part) and 3-4, 15-16, 18-41, 48-50.

DETAILED ACTION

1. Applicant's election with traverse of group 12, claims 1 (in-part), 2 and 5, directed to SEQ ID NOs: 97-99, in the reply filed on 8/30/04 is acknowledged. The traversal is on the ground(s) that group 25 (peptide cargo complexes) and group 38 (expression cassettes) are not distinct from group 12; and applicants argue that with the exception of groups 12, 25, 38, 50, 62, 74, 155, 168, 180 and 192, the restriction limits the subject matter of the invention to a single peptide. This is not found persuasive.

Examiner apologizes for the errors in numbering of the groups in the restriction requirement. It is noted that in the restriction requirement group 30 is a repetition of group 29; and also some of the groups were mis-numbered. The appendix with the correct numbering of groups provided by applicants is fully considered. Examiner appreciates the appendix provided by applicants.

It is noted that examiner has requested a species election of 'cargo' if group 25 is elected, however applicants failed to elect a single species of cargo in this application.

The elected group 12 is drawn to a peptide having an amino acid sequences SEQ ID NO: 97, 98 and 99, in which all the peptide sequences share the same common core structure (RRQRR); and group 25 invention is drawn to peptide-cargo complex of the peptides of group 12 (SEQ ID Nos; 97, 98, 99) with cargo. Applicants arguments regarding the group 25 to be examined along with the elected group 12 is persuasive, and claims 6-14, 17, 42, 45-47 (in-part) drawn to a peptide cargo complex and immunogen, in which the peptide has amino acid sequence of SEQ ID Nos: 97-99, will be joined with the elected group 12.

Applicants arguments that the group 38 examined together with the elected group 12 is not persuasive, since the group 38 inventions (claim 18-24) are drawn to expression cassette comprising a DNA encoding a fusion protein. Thus the inventions of group 38 are drawn to nucleic acid, which is structurally and functionally distinct from the elected group peptides, and belong to a different class of compounds. Thus, restriction between the two groups is proper and maintained.

Applicant's traversal of restriction to a single peptide has been fully considered and is not persuasive. The different peptides of SEQ ID Nos; 76-86 do not share a common core structure (i.e., common sequence) to group them together. Applicants argue that 'it is has been held that the Office may not impose a restriction requirement within a single claim' and cites *In re Watkinson* and *In re Haas*. *In re Watkinson* is related to reissue application and regarding failure to file a divisional application, and which is not an error correctable by reissue under 35 U.S.C. §251. *In re Haas* is whether rejection of non-elected claims Markush claims under 35 USC 121 is proper or not. None of these case laws are relevant to the current application. The instant claim 1 is not written as a generic claim as in applicant's arguments, in which by examining only the elected sequences would destroy the generic claim , and the generic claim is not examined to its merits. In the instant application, claim 1 is not considered as 'generic claim', in which examining only peptides of SEQ ID Nos 97-99 would destroy the invention. The claim does not recite a single common feature to link the different peptides into one single group. Applicant's arguments are not persuasive.

In this application examiner has made a restriction between independent and distinct inventions within an improper Markush group. The different peptides of groups 1-12 do not share a common core structure, thus restriction between the peptides is proper.

The requirement is still deemed proper and is therefore made FINAL.

Status of claims

2. Claims 1-50 (in-part) (peptide having amino acid sequences SEQ ID Nos 76-86, methods of use of the peptides), are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/30/04.

3. Claims 1, 2, 5, 6-14, 17, 42, 45-47 (in-part) (peptides having amino acid sequences of SEQ ID Nos 97-99, petide-cargo complexes, and immunogens), are currently being examined in this application.

Priority

4. This application is a CIP of application 09/653,182 filed on 8/31/00, which claims priority to provisional applications 60/151,980, and 60/188,944.

Information Disclosure Statement

5. The references cited in the Information Disclosure Statement filed on 9/3/02 have been considered.

Claim Objections

6. Claims 1, 2, 5, 6-14, 17, 42, 45-47 (in-part) objected to because of the following informalities: The claims recite the non-elected subject matter. Applicants are requested to amend the claim to remove the non-elected subject matter from the claims.

7. Claims 12 and 17 are objected to because of the following informalities: Both Claims 12 and 17 are dependent on claim 6, and recite exactly same limitations. Applicants are requested to either delete one of the claims or amend one of the claims, such that they are not duplicate of each other. Appropriate correction is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 2, 5, 6-11, 13, 42, 45-47 (in-part) are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0359347 A2 (Anderson et al).

The instant claims recite a peptide having amino acid sequence of SEQ ID NO: 97, 98 or 99, a peptide-cargo complex and an immunogen of the peptides.

Anderson et al teach covalently-linked complexes (CLCs) (refers to the instant peptide-cargo complex, and immunogen) for targeting a defined population of cells, comprising a targeting peptide; a cytotoxic agent. The reference teaches that the targeting protein useful in the invention is antibodies, peptides, drugs, cytotoxic peptides such as antiviral proteins (refers to the instant claim apoptotic proteins) (i.e., see the list of ~~parting~~ targeting moieties listed in page 4). The reference teaches that peptides or analogs that include a sequence present in the highly basic region, such as CFITKALGISYGRKK**RRQRR**RPPQGS (refers to the instant claim peptide having an amino acid sequence of RRQRR(SEQ ID NO:97)) are conjugated to targeting protein conjugates to aid in internalization and targeting to nucleus (i.e., see page 7). The reference clearly anticipates the claimed invention.

10. Claims 1, 2, 5, 6-11, 42, 45-47 (in-part) are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0656950 B1 (Barsoum et al).

The instant claims recite a peptide having amino acid sequence of SEQ ID NO: 97, 98 or 99, a peptide-cargo complex and an immunogen of the peptides.

Barsoum et al teach delivery of biologically active cargo molecules, such as polypeptides, nucleic acids into the cytoplasm and nucleus of cells *in vitro* and *in vivo*. The reference teaches that the intracellular delivery of cargo molecules according to this invention is accomplished by the use of novel transport polypeptides, which comprise portions of HIV, tat protein and covalently attached to cargo molecules. (i.e., see page 2). The reference teaches transport polypeptides have tat 37-72 (SEQ ID NO: 2), tat37-58 (SEQ ID NO:3), tat38-58GGC (SEQ ID NO: 4), tatCGG47-58 (SEQ ID NO: 5), and tat47-58GGC (SEQ ID NO: 6) (all these sequences

(SEQ ID Nos 2-6) have RRQRR sequence), and read on the instant claim peptides. The reference teaches that the cargo can be either peptides, nucleic acids, drugs, or receptors, kinase inhibitors. The reference teaches delivery of cargo to the cytoplasm of the cells and further to nucleus of target cells. Thus, the reference clearly anticipates the claimed invention.

11. Claims 1, 2, 5, 6-7, 9-11, 42, 45-47 (in-part) are rejected under 35 U.S.C. 102(b) as being anticipated by Vives et al (Letters in Peptide Science, 4 (1997) 429-436).

The instant claims recite a peptide having amino acid sequence of SEQ ID NO: 97, 98 or 99, a peptide-cargo complex and an immunogen of the peptides.

Vives et al teach peptide 37-72 from HIV-1 tat allows internalization of conjugated proteins. The reference teaches various modified peptides of tat (see table 1) used in the method. All the modified tat proteins have RRQRR sequence of the instant claimed peptide sequence. Thus the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 2, 5, 6-14, 17, 42, 45-47 (in-part) are rejected under 35 U.S.C. 103(a) as being unpatentable over by either EP 0359347 A2 (Anderson et al) or EP 0656950 B1 (Barsoum et al) or Vives et al (Letters in Peptide Science, 4 (1997) 429-436) and Pardridge et al (US Patent 6,287,792, filing date June 17, 1991).

EP 0359347 A2 (Anderson et al), Barsoum et al (EP 0656950 B1) and Vives et al have been discussed supra. Anderson et al teach covalently-linked complexes (CLCs) (refers to the instant peptide-cargo complex, and immunogen) for targeting a defined population of cells, comprising a targeting peptide; a cytotoxic agent. Barsoum et al teach delivery of biologically active cargo molecules, such as polypeptides, nucleic acids into the cytoplasm and nucleus of cells *in vitro* and *in vivo*. Vives et al teach peptide 37-72 from HIV-1 tat allows internalization of conjugated proteins. Neither Anderson et al or Barsoum et al nor Vives et al teach that the peptide is biotinylated and the cargo is avidin labeled. Pardridge et al teach compositions for delivering an agent into cells in vitro or tissues or organisms in vivo. The reference teaches that the composition comprises either avidin or avidin fusion protein as a transporter vector bonded to a biotinylated agent to form an avidin-biotin-agent complex. The reference teaches that the transporter vector further comprises a targeting moiety bound to the avidin moiety (refers to the instant claim 'cargo is avidin labeled') (i.e., see column 3). The reference teaches advantages of biotinylation of peptides (i.e., see column 3 bridging the column 4) (refers to the instant claim limitation peptide is biotinylated). The reference teaches that the targeting moiety can be insulin or anti-

receptor antibodies or cationized proteins or lectins (i.e., see column 4) (refers to instant claims 'cargo'). The reference teaches that the avidin-biotin bond is one of the highest affinity binding reactions found in nature with a molar dissociation constant of 10^{-15} M, and t1/2 of ligand dissociation 89 days; and avidin-biotin bond is stable in serum and in circulation. The reference teaches that peptides may be biotinylated chemically using activated biotin analogs, and recombinant methods of making biotinylated proteins, avidin linked fusion proteins.

Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the avidin-biotin as labeling or linking molecules to the peptide-cargo complexes of the instant invention, since Pardridge et al teach the advantages of linking the peptides to biotin and then link the avidin labeled peptides to use as transporter vectors. A person skilled in the art would have been motivated to use the avidin-biotin bond since it has the highest affinity binding reactions, and the biotin-avidin bond is most stable in serum and in circulation, such that drugs can be targeted and delivered to the target tissue to produce pharmacological activity.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

29 November 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER